IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
REQUEST FOR FILING NATIONAL PHASE OF
PCT APPLICATION UNDER 35 U.S.C. 371 AND 37 CFR 1.494 OR 1.495

To: Hon. Commissioner of Patents
Washington, D.C. 20231

09/889827

00909

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

Atty Dkt: P 282714 /O7852WO
M# /Client Ref.

From: Pillsbury Winthrop LLP, IP Group: Date: MONDAY, July 23, 2001

This is a **REQUEST** for **FILING** a PCT/USA National Phase Application based on:

1. International Application	2. International Filing Date	3. Earliest Priority Date Claimed
PCT/GB00/00163	21 JAN 2000	22 JAN 1999
⇧ country code	Day MONTH Year	Day MONTH Year (use item 2 if no earlier priority)

4. Measured from the earliest priority date in item 3, this PCT/USA National Phase Application Request is being filed within:

(a) ☐ 20 months from above item 3 date (b) ☒ 30 months from above item 3 date,

(c) Therefore, the due date (unextendable) is July 22, 2001

5. Title of Invention PROCESS FOR PRODUCING GRANULES

6. Inventor(s) MISSELBROOK, John

Applicant herewith submits the following under 35 U.S.C. 371 to effect filing:

7. ☒ Please immediately start national examination procedures (35 U.S.C. 371 (f)).

8. ☒ **A copy of the International Application** as filed (35 U.S.C. 371(c)(2)) is transmitted herewith (file if in English but, if in foreign language, file only if not transmitted to PTO by the International Bureau) including:

a. ☐ Request;
b. ☒ Abstract;
c. 20 pgs. Spec. and Claims;
d. - sheet(s) Drawing which are ☐ informal ☐ formal of size ☐ A4 ☐ 11"

9. ☒ **A copy of the International Application has been transmitted by the International Bureau.**

10. **A translation of the International Application** into English (35 U.S.C. 371(c)(2))
a. ☐ is transmitted herewith including: (1) ☐ Request; (2) ☐ Abstract;
(3) _____ pgs. Spec. and Claims;
(4) _____ sheet(s) Drawing which are:
☐ informal ☐ formal of size ☐ A4 ☐ 11"
b. ☐ is not required, as the application was filed in English.
c. ☐ is not herewith, but will be filed when required by the forthcoming PTO Missing Requirements Notice per Rule 494(c) if box 4(a) is X'd or Rule 495(c) if box 4(b) is X'd.
d. ☐ Translation verification attached (not required now).

11. ☒ Please see the attached Preliminary Amendment

12. ☐ Amendments to the claims of the International Application **under PCT Article 19 (35 U.S.C. 371(c)(3)), i.e., before 18th month from first priority date above in item 3, are transmitted herewith (file only if in English) including:**

13. ☒ PCT Article 19 claim amendments (if any) have been transmitted by the International Bureau

14. ☐ Translation of the amendments to the claims **under PCT Article 19 (35 U.S.C. 371(c)(3)), i.e., of claim amendments** made before 18th month, **is attached (required by 20th month from the date in item 3 if box 4(a) above is X'd, or 30th month if box 4(b) is X'd, or else amendments will be considered canceled).**

15. **A declaration of the inventor** (35 U.S.C. 371(c)(4))
a. ☐ is submitted herewith ☐ Original ☐ Facsimile/Copy
b. ☒ is not herewith, but will be filed when required by the forthcoming PTO Missing Requirements Notice per Rule 494(c) if box 4(a) is X'd or Rule 495(c) if box 4(b) is X'd.

16. **An International Search Report (ISR):**
a. Was prepared by ☒ European Patent Office ☐ Japanese Patent Office ☐ Other
b. ☒ has been transmitted by the international Bureau to PTO.
c. ☒ copy herewith (2 pg(s).) ☒ plus Annex of family members (2 pg(s).).

17. **International Preliminary Examination Report** (IPER):
a. ☒ has been transmitted (if this letter is filed after 28 months from date in item 3) in English by the International Bureau with Annexes (if any) in original language.
b. ☒ copy herewith in English.
c.1 ☐ IPER Annex(es) in original language ("Annexes" are amendments made to claims/spec/drawings during Examination) including attached amended:
c.2 ☐ Specification/claim pages #_____ claims #
Dwg Sheets #
d. ☐ Translation of Annex(es) to IPER **(required by 30th month due date, or else annexed amendments will be considered canceled).**

18. **Information Disclosure Statement** including:
a. ☒ Attached Form PTO-1449 listing documents
b. ☐ Attached copies of documents listed on Form PTO-1449
c. ☒ A concise explanation of relevance of ISR references is given in the ISR.

19. ☐ **Assignment** document and Cover Sheet for recording are attached. Please mail the recorded assignment document back to the person whose signature, name and address appear at the end of this letter.

20. ☐ Copy of Power to IA agent.

21. ☐ **Drawings** (complete only if 8d or 10a(4) not completed): ___ sheet(s) per set: ☐ 1 set informal; ☐ Formal of size ☐ A4 ☐ 11"

22. Small Entity Status ☐ is **Not** claimed ☒ is claimed (**pre**-filing confirmation required)
22(a) _____ (No.) Small Entity Statement(s) enclosed (since 9/8/00 Small Entity Statements(s) not essential to make claim)

23. **Priority** is hereby claimed under 35 U.S.C. 119/365 based on the priority claim and the certified copy, both filed in the International Application during the international stage based on the filing in (country) Great Britain of:

	Application No.	Filing Date		Application No.	Filing Date
(1)	9901479.7	22 JAN 1999	(2)		
(3)			(4)		
(5)			(6)		

a. ☒ See Form PCT/IB/304 sent to US/DO with copy of priority documents. If copy has not been received, please proceed promptly to obtain same from the IB.
b. ☐ Copy of Form PCT/IB/304 attached.

RE: USA National Phase Filing of PCT/ /

JC17 Rec'd PCT/PTO 23 JUL 2001

24. Attached: Client Correspondence indicating Change of Applicant

25 Per Item 17.c2, **cancel original** pages #_____, claims #_____, Drawing Sheets #

26. **Calculation of the U.S. National Fee (35 U.S.C. 371 (c)(1)) and other fees is as follows:**

Based on amended claim(s) per above item(s) ☐ 12, ☐ 14, ☐ 17, ☐ 25 (hilite)

Total Effective Claims	minus 20 =	x $18/$9	=	$0	966/967
Independent Claims	minus 3 =	x $80/$40	=	$0	964/965
If any proper (ignore improper) Multiple Dependent claim is present,		add$270/$135		+0	968/969

BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(4)): →→ **BASIC FEE REQUIRED, NOW** →→→→

A. If country code letters in item 1 are **not** "US","BR","BB","TT","MX","IL" "NZ", "IN" or "ZA"

See item 16 re:

1.	Search Report was not prepared by EPO or JPO - - - - - - - - -	add$1000/$500		960/961
2.	Search Report was prepared by EPO or JPO - - - - - - - - - - - -	add$860/$430	+430	970/971

SKIP B, C, D AND E UNLESS country code letters in item 1 are "US","BR","BB","TT","MX","IL", "NZ", "IN" or "ZA"

(X) →	☐	B.	If USPTO did not issue both International Search Report (ISR) and (if box 4(b) above is X'd) the International Examination Report (IPER), - - - - - - - - - - - - - - - - - - -	add$1000/$500	+0	960/961
(only) (one) → (of)	☐	C.	If USPTO issued ISR but not IPER (or box 4(a) above is X'd), -	add$710/$355	+0	958/959
(these) (4) → (boxes)	☐	D.	If USPTO issued IPER but IPER Sec. V boxes not all 3 YES, -	add$690/$345	+0	956/957
→	☐	E.	If international preliminary examination fee was paid to USPTO and Rules 492(a)(4) and 496(b) satisfied (IPER Sec. V all 3 boxes YES for all claims), - - - - - - - - - - - - -	add $100/$50	+0	962/963

27. **SUBTOTAL =** $430

28. If Assignment box 19 above is X'd, add Assignment Recording fee of ----$40 +0 (581)

29. Attached is a check to cover the - **TOTAL FEES** $430

Our Deposit Account No. 03-3975

Our Order No. 11765 (C#) | 282714 (M#)

00909

CHARGE STATEMENT: The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, or asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 and 492 (missing or insufficient fee only) now or hereafter relative to this application and the resulting Official document under Rule 20, or credit any overpayment, to our Account/Order Nos. shown above for which purpose a duplicate copy of this sheet is attached.

This CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee transmittal form is filed

Pillsbury Winthrop LLP
Intellectual Property Group

By Atty: Paul N. Kokulis **Reg. No.** 16773

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NOTE: File in duplicate with 2 postcard receipts (PAT-103) & attachments.

09/889827
JC17 Rec'd PCT/PTO 23 JUL 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION OF

Inventor(s): MISSELBROOK, John

Filed: Herewith

Title: PROCESS FOR PRODUCING GRANULES

JULY 23, 2001

PRELIMINARY AMENDMENT

Hon. Commissioner of Patents
Washington, D.C. 20231

Sir:

Please amend this application as follows:

IN THE SPECIFICATION:

At the top of the first page, just under the title, insert

☒ --This application is the National Phase of International Application PCT/GB00/00163 filed January 21, 2000 which designated the U.S. and that International Application

☒ was ☐ was not published under PCT Article 21(2) in English.--

Respectfully submitted,

PILLSBURY WINTHROP LLP
Intellectual Property Group

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PROCESS FOR PRODUCING GRANULES

This invention relates to a process for the production of granules, in particular water dispersible and water soluble granules. More particularly it relates to an extrusion process for the production of water dispersible granules. The invention is especially useful in the production of granules containing biologically active compounds and other substances and in particular, agrochemical products, for example pesticides.

Dispersible granule formulations of pesticides are known and have certain advantages. In particular, such granules are advantageous due to their ease of handling and reduced worker exposure compared to powder or liquid formulations and also due to their compatibility, comparative cost. Furthermore, environmentally friendly packaging may be used and the presence of inert materials also has environmental advantages. G. A. Bell, "Chemistry and Technology of Agrochemical Formulations", Edited by D. A. Knowles (Kluver, 1998), pages 80-114, describes a range of dispersible granule types and processes for their manufacture.

WO 89/00079 describes a process for the preparation of water dispersible granules which comprises mixing the desired ingredients of the granules to form an extrudable wet mix which has a dough-like consistency, that is, a consistency analogous to a stiff dough produced in the bread making process. Such dough-like consistency may be provided by thorough mixing or kneading using a mixing apparatus such as a pug mill, double shafted auger, or an extrusion apparatus may be adapted to provide suitable mixing. It also requires that after extrusion the wet extrusions are broken down by rolling, preferably in a tumbling action. However, the rolling action required following extrusion may cause the formation of a "shell" of

compacted material on the outside of the granule that leads to an increase in the drying time/temperature. EP-A- 0484 147 1 describes a process for preparing dispersible propanil granules. Propanil is N-(3,4-dichlorophenyl)propionamide. It is known that propanil may degrade during processing or have poor stability due to its low melting point. The process disclosed in EP-A-484 147 comprises the steps in sequence of combining one or more surfactants with propanil and milling to a particle size of less than 20 microns to form a premix, adding less than 25 percent by weight water and optionally a wetting agent to said premix and mixing until a paste is obtained granulating said paste thereby producing granules and drying said granules. This process is said to overcome certain difficulties in the processing of propanil due to its low melting point and tendency to become sticky during processing.

However, propanil, in addition to having a relatively low melting point , is also prone to hydrolysis. The formation of a paste containing water may lead to further difficulties as regards stability during processing if the energy input during the paste formation is too high. Thus, the above described processes may impose a number of constraints on the ingredients by limiting the choice of available components to those which are not heat sensitive which may be included in the granules due to the physical or chemical nature of those ingredients. In particular, the energy input required in the formation of the dough or paste may degrade certain low-melting, or temperature-sensitive, active materials. Water-soluble or slightly-soluble actives may form crystal bridges which, on addition to water, inhibit the rapid and desirably complete dissolution or disintegration of the granules to their primary particle size prior to granulation.

The handling of a dough or paste in a manufacturing plant can also cause processing problems. In particular difficulties may arise due to variation in the viscosity of the dough or paste caused by temperature and/or shear conditions. This factor may lead to variation in product quality and yield and may cause fouling or blockages in the process apparatus.

There remains a need for improvements to existing known processes of preparing granules that are dispersible and/or soluble in water to allow sensitive components to be included in formulations and to avoid or reduce processing problems for example due to fouling or blockage. Furthermore, granules providing excellent delivery of the active to the point of use including good dispersibility are desired. In addition physical properties such as ease of handling, low friability so as to reduce or minimise the dust content are also desirable for reasons of health and safety and ease of product distribution.

It has been found that acceptable granules may be produced by a process involving forming a pre-mix of the components of the granule and extruding the pre-mix provided that a paste is not formed during the preparation of the pre-mix which is to be extruded.

In a first aspect the invention provides a process for the production of water dispersible granules comprising, preparing a pre-mix in the form of a free-flowing powder, preferably a homogeneous powder, comprising an active material and an excipient and optionally other components, with at least one component of the pre-mix being liquid without forming a paste, and extruding the pre-mix in an extruder, for example a low pressure extruder to form the granules. The excipient may be

liquid in which case an additional liquid component is not required although a further liquid component may be included as desired

WO 96/25828 describes an apparatus and a method for extrusion which eliminates the undesirable effect of the ingress of pastes, which form as the moist finely divided, water-insoluble powders are forced through the screen of conventional, low-pressure extruders.

It has been surprisingly found that granules that are water-dispersible and/or water-soluble can be produced using the process according to the invention and they provide excellent delivery of the active to the crop to be treated. Further, the granules produced by a process according to this invention , exhibit improved characteristics as compared to granules formed by process of the prior art on storage, dilution and in use.

The process involves the initial preparation of a pre-mix comprising the active material together with at least one excipient in the form of a free-flowing, powder. Desirably the premix is a homogeneous powder. The pre-mix is preferably prepared by the absorption of a liquid for example water, or any other suitable liquid onto an active solid material, which is preferably finely divided. The active solid may be mixed with an excipient preferably a surfactant for example a dispersant and a wetting agent, a filler, a disintegrant, a stabiliser, a flow aid and the likeand mixtures thereof. It is especially preferred that the pre-mix comprises an active, an excipient comprising a dispersant and water. It is also preferred that the granule obtained from the process contains these components. In a preferred embodiment, the active material is suitably milled either prior to the addition of the excipient or milled together with it.

Suitably the premix is formed by the application of shear especially in a blending step or a milling step and optimally in one or more blending steps and one or more milling steps. Suitable apparatus for the blending step(s) include a low-shear, high intensity blender such as a Lodige Ploughshare mixer, ribbon, Y-cone, double cone or trough blender, so that a free-flowing powder is formed. The premix is fed directly or indirectly into a suitable low-pressure extruder, such as that described in WO 96/26828, so that the premix is compacted against the apertures in the screen and forced through. The composition of the premix and the extruder settings are such that the formation of a paste before extrusion is avoided The powder premix which is fed to an extruder is converted into a compacted solid extrudate which can be collected as a free-flowing granule.

In the present process the material being processed remains a free flowing particulate material during the formation of the pre-mix. In particular, the material does not form a paste prior to extrusion. However, as the composition contains one or more liquid components, it may be wet or dry provided that it remains free-flowing and particulate during the process. The particles of the material are of such a composition that they are able to move relative to one another and do not, to any significant extent, agglomerate into lumps and remain as lumps having a particle size of at least several times that of the bulk of the particulate material being processed during the formation of the pre-mix. If any lumps are formed during this part of the process, the process conditions for formation of the premix and/or the composition of the premix should be varied so that the lumps disintegrate into finer particles on application of shear. If any such lumps or agglomerates are formed, it is especially preferred that the agglomerate is of such a composition and physical

structure that it disintegrates into finer particles on the application of manual force by rubbing between the fingers

In the context of the present invention, a paste may be considered as a mass of material, for example an agglomerate, which contains sufficient liquid or is at such a temperature that the particulate material being processed forms into an agglomerate which is mouldable or deformable and which is not free-flowing. Thus, a paste does not disintegrate into finer particles on application of shear, for example by rubbing between fingers, but rather remains as an agglomerated mass and the shear acts to mould or deform the agglomerate.

Depending on the components selected for producing the granules, the relative amounts of those components are selected and the process conditions for example the level of shear are selected so as to avoid the formation of a paste prior to extrusion.

After the extrusion step in the process, the granules so formed may be processed further as desired, for example by drying and by sieving or other size-classification steps. In a preferred embodiment of the invention, the granules are dried. The granules may be dried by any suitable equipment, for example, a fluid-bed drier and a tray dryer. As a further preferred process step, the granules are classified by size, for example, sieved so as to remove under- and over-size material. In a preferred embodiment, the extruded material is suitably dried and size-classified. It is especially preferred that the process of the present invention does not involve a rolling process step in which the extruded material is treated.

In the process of the present invention, uniform, free-flowing granules are produced with excellent properties including uniform bulk density, lack of dust, resistance to attrition and rapid disintegration in water to form a suspension or solution of the active ingredient on use. In a preferred embodiment, over 90%, especially 99% of the granules, prior to sieving or screening, are of a suitable size such that further processing to alter the size of the granules is not required. .

Avoiding the formation of a paste during the process prior to extrusion affords further advantages in that flexibility in the range of actives and other components which may be selected is increased as compared to processes in which a paste is formed. This permits the selection of actives and other ingredients which otherwise may not be suitable due to introducing processing difficulties. Thus any detrimental effects due to the formation of a paste on the ingredients, and vice-versa, are no longer a factor. Ingredients can thus be chosen that produce optimum product properties whether in use or otherwise, for instance in distribution, rather than the choice being compromised due to processing considerations.

The premix is suitably prepared by blending two or more materials; for example the active and the excipient and/or the liquid component, for a period of at least 30 seconds, preferably 1 to 15 minutes, more preferably 1 to 10 minutes and especially 2 to 5 minutes.

The solid component may be milled to an appropriate particle size prior to blending with other components. Preferably, milling is carried out after blending so the blended materials are milled to a desired particle size. Milling may be carried out by any suitable means although air milling is preferred. Suitably air milling is carried out

at an air pressure of at least 2 bar and desirably at least 5 bar. Suitably, the milled material has a particle size of 2 to 30 microns and desirably 4 to 20 microns.

As desired one or more blending steps may be carried out after the milling step if desired Such a blending step may be carried out for at least 30 seconds, preferably for 1 to 15 minutes and especially for 1 to 10 minutes. The one or more blending step may be carried out under low shear or desirably high shear conditions. Where more than one blending step is employed, it is preferred that the material being processed is subjected to high shear in the first blending step and low or moderate shear in a subsequent blending step.

The liquid component may be added to the milled material, either a blend or a single component product, or it may be added to a solid component in a blending step prior to or after the milling step. The liquid may be added in any suitable manner although it is preferred that the liquid be added as a spray in order to reduce the risk of agglomerates or lumps forming in the premix.

It is essential in the formation of the pre-mix that the steps in the formation are carried out under such conditions and for a period such that a paste is not formed.

The process may be employed to produce granules comprising a wide range of active ingredients. By way of example, the process of the invention may be employed to produce granules comprising, as the active , a pharmaceutical, an agricultural chemical, an oil field chemical, an animal feedstuff, a dyestuff, and a detergent.Granules comprising other types of active may also be produced by a process according to the invention.The process is particularly suitable for, but not limited to, the production of granules comprising an agricultural chemical.

Examples of agricultural chemicals which may be employed as the active include abamectin, imidazolinone, ametryn, amitaz, atrazine, azoxystrobin, benomyl, bensulfuron-methyl, bentazone, bifenox, bromoxynil, captan, carbendazim, carfentrazone-ethyl, chloridazon, chlorothalonil, chlortoluron, chlorsulfuron, cinosulfuron, clodinafop, clopyralid, lambda-cyhalothrin, cyhexatin, cymoxynil, alpha-cypermethrin, deltamethrin, diflufenican, dimethomorph, diuron, ethofumesate, emamectin benzoate, fibronil, flurtamone, glyphosate, imazamethabenz-methyl, imazapyr, imazethapyr, imadaclopfid.isoproturon, linuron, mancozeb, maneb, metamitron, methiocarb, metribuzin, metsulfuron-methyl, milbectin, nicosulfuron, oxadixyl, oxyfluorfen, phenmedipham, pirimisulfuron-methyl, propanil, propyzamide, rimsulfuron, simazine, sulfometuron,-methyl, thifensulfuron-methyl, thiram, tribenuron-methyl, and triflusulfuron-methyl.

Suitable excipients include surface active agents (surfactants) including wetting agents and dispersing agents or a combination of both and flow agents.

Examples of suitable wetting agents include: alkali metal, for example sodium, salts of alkyl aryl sulphonates, alkyl aryl sulphosuccinates, and alkyl sulphates.

Examples of dispersing agents include sodium lignosulphonates, sodiumnaphthalene sulphonate formaldehyde condensates, tristyrylphenol ethoxylate phosphate esters, aliphatic alcohol ethoxylates, alkylphenol ethoxylates, copolymers, random and block, of ethylene oxide and propylene oxide , "comb" graft copolymers and polyvinyl alcohol-vinyl acetate copolymers.

Suitable other excipients include disintegrants for example: Bentonite, modified starch and polyvinyl pyrrolidone:stabilisers, for example citric acid, polyethylene glycol and butylated hydroxy toluene; and fillers, for example, starch, lactose, china clay, sucrose and kaolin.

In addition to the active material and the excipient and liquid component, further ingredients, for example further excipients, may be fed to the process at any point, including before, during or after addition of the liquid component to the process, just prior to or during the extrusion step. However, if further ingredients are to be added, it is especially preferred that they be added to the process prior to extrusion and optimally be mixed with the active component prior to or with the addition of the liquid component. Suitable further ingredients include surfactants including dispersants and wetting agents, fillers, disintegrants, stabilisers and flow-aids. The important factor in the choice of a further ingredient and the amount of the ingredient is that it does not lead to the formation of a dough or paste during the process for example due to significant particle-to-particle interaction..

In an especially preferred embodiment of the invention, the active comprises propanil and the excipients comprise one or more of a disintegrant, a flow agent a filler and a surfactant. In a further preferred embodiment, the propanil is mixed with the disintegrant and flow agent, preferably by air milling, surfactant is then added to the mixture and then water is added to the mixture so as to form a free-flowing generally homogeneous powder, that is a particulate material. In an alternative embodiment, the propanil is blended with a surfactant, a disintegrant and a filler and then milled and water is added to the mixture after milling in a further blending step to produce a free-flowing generally homogeneous powder. The pre-mix powder is then extruded by passing through an extruder, preferably an extruder and extrusion

process as described in WO 96/26828. The granules resulting from the extrusion process suitably have a thickness or particle size of 0.1 to 5mm, preferably 0.3 to 2mm and especially 0.5 to 1.5mm. The granules are then suitably dried and optionally classified by sieving.

The invention provides a novel granular composition comprising an agricultural active and an excipient obtainable by a process according to the first aspect of the invention.

The invention is illustrated by the following examples but is in no way limited by them:

EXAMPLE I

The following formulation was prepared:

Propanil		80%
Sodium alkyl aryl sulphonate		1.0%
Sodium Lignosulphonate		10.0%
Potato Starch		1.0%
China Clay	to	100%

The above formulation was prepared by first blending the Propanil Technical, china clay and starch in a Ploughshare blender for 5 minutes. The blend thus formed was then air milled to an average particle size of 5-7 microns. Water was added to the air milled premix in a Ploughshare blender until a water content of approx. 18% was obtained. Formation of a paste was avoided in preparing the premix. The free-flowing powder obtained was fed to a basket extruder. A low pressure extruder as set out in WO-A-96/26828 was used to extrude the premix. A compacted solid extrudate was obtained, which was dried at 65°C for 15 minutes until a moisture content of below 1.5% was obtained.

The granules were tested as follows:-

1 g of the granules were added to a measuring cylinder containing 100 mls of water. The cylinder was inverted through 180 degrees and back again for one full inversion, taking 2 seconds and the number of seconds for complete disintegration observed. The cylinder was then allowed to stand for 30 minutes, undisturbed, and a 10 ml sample taken from the centre of the cylinder and analysed, gravimetrically, for the amount of solids present. This figurewas then used to calculate the % of material in suspension after standing for this time. The results were compared to two commercial formulations of Propanil, one (STAM® 80 EDF) manufactured by a standard extrusion technique invoiving the formulation of a paste and the other (WHAM® 80DF) by pan granulation. The results obtained were as follows:-

Commercial Product	Time Taken for Product to Disintegrate	% Remaining in Suspension after 30 minutes

Stam® 80 EDF	3 - 5 minutes	71.3
Wham® 80 DF	> 5 minutes	9.9
Example 1	< 1 minute	86.9

The above results indicate the advantages of the product produced by the process described in this invention. In addition it was noted that the standard extruded product, Stam® 80 EDF was badly caked in the commercial pack, indicating a physical degradation of the product on storage.

EXAMPLE 2

The following formulation was prepared:

Chlorsulfuron		75%
Sodium alkyl aryl sulphonate		1%
Sodium lignosulphonate		12.5%
China Clay	to	100%

The above formulation was prepared by first blending the Chlorsulfuron Technical and china clay in a Ploughshare blender for 5 minutes. The blend thus formed was then air milled to an average particle size of 3-4 microns. Water was added to the air milled premix in a Ploughshare blender until a water content of approx. 14.5% was obtained. Formation of a paste was avoided. The free-flowing powder was extruded in an extruder as described in WO96/26828. A compacted solid extrudate was obtained, which was dried at 60°C for 15 minutes until a moisture content of 0.9% was obtained. The granules were tested by the method set out in Example 1.

The results were compared to a commercial formulation of chlorsulfuron, (GLEAN® 75 DF) manufactured by a standard fluid bed agglomeration. The results obtained were as follows:-

Commercial Product	Product to Disintegrate	Time Taken for% Suspension after 30 minutes Remaining in
Glean® 75 DF	< 1 minute	69
Example 2	< 1 minute	86

It was noted that the Glean® sample was much more dusty than the extruded sample produced by the process of the present invention. At the low use rate of the product, the higher suspensibility for the product would lead to a higher availability in field use and a higher efficacy.

The results were compared to a commercial formulation of chlorsulfuron. (GLEAN® 75 DF) manufactured by a standard fluid bed agglomeration. The results obtained were as follows:-

Commercial Product	Time Taken for Product to Disintegrate	% Remaining in Suspension after 30 minutes
Glean® 75 DF	< 1 minute	69
Example 2	< 1 minute	86

It was noted that the Glean® sample was much more dusty than the extruded sample produced by the process of the present invention. At the low use rate of the product, the higher suspensibility for the product would lead to a higher availability in field use and a higher efficacy.

EXAMPLE 3

A commercial premix of Chloridazon 65 DF was obtained from which a commercial sample of water dispersible granule had been produced by a wet agglomeration technique.

The same premix was formed into granules using the process of the present invention and both samples were tested for suspensibility as set out in Example 1. The results obtained are as follows:-

	% Suspensibility
Commercial Chloridazon 65 DF	89
Example 3	98

EXAMPLE 4

The following formulation was prepared by a process according to the present invention:

Captan	80.0 %
Sodium alkyl aryl sulphonate	1.0 %
Sodium naphthalene formaldehyde condensate	2.0 %
Silica	3.0 %
Kaolin	to 100 %

Zeta Potential Measurements may be used to evaluate the micro-electrophoretic mobility of active ingredient particles and accordingly derive the Zeta Potential of those particles. This allows preferred surfactants, in particular anionic, non-ionic and cationic dispersants. for water dispersible granules of the active ingredient to be selected so as to identify the most appropriate candidate dispersants. It is preferred

that the dispersants give a Zeta Potential measurement of about 0 mV for a non-ionic surfactant and in excess of approximately - 30 mV for an anionic surfactant and in excess of approximately + 30 mV for a cationic surfactant.

The active material is suitably present at a level of at least 50 %, preferably from 60 to 90% by weight of the granule. The excipient is suitably present at a level of less than 50%, preferably from 10 to 30% by weight of the granule. The liquid, preferably water, content of the granule is suitably less than 10% and preferably from 0.1 to 5% by weight of the granule

CLAIMS

1. A process for the production of water dispersible granules comprising, preparing a pre-mix in the form of a free-flowing powder comprising an active material and an excipient with at least one component of the pre-mix being liquid, without forming a paste, and extruding the pre-mix to form the water dispersible granules.

2. A process according to claim 1 in which a liquid is adsorbed onto an active solid material.

3. A process according to any one of the preceding claims in which the pre-mix is a homogeneous powder.

4. A process according to any one of the preceding claims in which the premix is formed by the application of shear.

5. A process according to any one of the preceding claims in which the pre-mix comprises an active material and an excipient selected from a surfactant, a filler, a disintegrant, a stabiliser, a flow aid and mixtures thereof.

6. A process according to any one of the preceding claims which comprises preparing the pre-mix in a blending step and optionally in a milling step.

7. A process according to claim 6 in which the blending step is carried out for a period of at least 30 seconds.

8. A process according to any one of claims 6 or 7 which comprises feeding the active material to a blending step, passing the blended material to a milling step so as to reduce the particle size of the blended material and passing the milled material to a further blending step to produce the pre-mix.

9. A process according to claim 8 in which the first blending step is conducted under conditions of high shear and the second blending step is conducted under conditions of low or moderate shear

10. A process according to any one of claims 6 to 9 in which the active material and an excipient selected from a disintegrant, a filler and a surfactant and mixtures thereof are blended in a blending step.

11. A process according to any one of claims 6 to 10 in which a liquid and optionally a further excipient selected from a surfactant, a disintegrant and a filler are added to the process in a second or subsequent blending step.

12. A process according to any one of the preceding claims in which the liquid is added as a spray.

13. A process according to any one of the preceding claims which further comprises drying and optionally size classifying the extruded material.

14. A process according to any one of the preceding claims in which the active material is selected from, a pharmaceutical, an agricultural chemical, an oil field chemical, an animal feedstuff, a dyestuff, and a detergent.

15. A process according to any one of the preceding claims in which the active material is an agricultural chemical and is selected from, bensulfuron-methyl, captan, chloridazon, chlorsulfuron, glyphosate, oxyfluorfen and propanil.

16. A process according to any one of the preceding claims in which the pre-mix comprises a surfactant selected from alkyl aryl sulphonates, alkyl aryl sulphosuccinates, alkyl sulphates and lignosulphonates.

17. A process according to any one of the preceding claims in which the granule comprises propanil and excipients comprising an alkyl aryl sulphonate, a lignosulphonates, a disintegrant and a filler.

18. A granular composition comprising an agricultural active and an excipient obtainable by a process according to any one of claims 1 to 17.

FOR UTILITY/DESIGN
CIP/PCT NATIONAL/PLANT
ORIGINAL/SUBSTITUTE/SUPPLEMENTAL
DECLARATIONS

RULE 63 (37 C.F.R. 1.63) DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PW
FORM

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name, and I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the **INVENTION ENTITLED PROCESS FOR PRODUCING GRANULES**

the specification of which (CHECK applicable BOX(ES))

X A ☐ is attached hereto.

BOX(ES) → B. ☒ was filed on July 23, 2001 as U.S. Application No. 09/889,827

→ → C. ☒ was filed as PCT International Application No. PCT/ GB00/00163 on January 21, 2000

and (if applicable to U.S. or PCT application) was amended on

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose all information known to me to be material to patentability as defined in 37 C F R. 1.56 Except as noted below, I hereby claim foreign priority benefits under 35 U S C. 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT International Application which designated at least one other country than the United States, listed below and have also identified below any foreign application for patent or inventor's certificate, or PCT International Application, filed by me or my assignee disclosing the subject matter claimed in this application and having a filing date (1) before that of the application on which priority is claimed, or (2) if no priority claimed, before the filing date of this application

PRIOR FOREIGN APPLICATION(S) Number	Country	Day/MONTH/Year Filed	Date first Laid-open or Published	Date Patented or Granted	Priority NOT Claimed
9901479.7	Great Britain	22 January 1999			

If more prior foreign applications, X box *at bottom* and continue on attached page.

Except as noted below, I hereby claim domestic priority benefit under 35 U S C 119(e) or 120 and/or 365(c) of the indicated United States applications listed below and PCT international applications listed above or below and, if this is a continuation-in-part (CIP) application, insofar as the subject matter disclosed and claimed in this application is in addition to that disclosed in such prior applications, I acknowledge the duty to disclose all information known to me to be material to patentability as defined in 37 C F R 1.56 which became available between the filing date of each such prior application and the national or PCT international filing date of this application:

PRIOR U.S. PROVISIONAL, NONPROVISIONAL AND/OR PCT APPLICATION(S) Application No. (series code/serial no.)	Day/MONTH/Year Filed	Status pending, abandoned, patented	Priority NOT Claimed

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

And I hereby appoint Pillsbury Winthrop LLP, Intellectual Property Group, telephone number (703) 905-2000 (to whom all communications are to be directed), and persons of that firm who are associated with USPTO Customer No 909 (see below label) individually and collectively my attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith and with the resulting patent, and I hereby authorize them to delete from that Customer No names of persons no longer with their firm, to add new persons of their Firm to that Customer No., and to act and rely on instructions from and communicate directly with the person/assignee/attorney/firm/ organization who/which first sends/sent this case to them and by whom/which I hereby declare that I have consented after full disclosure to be represented unless/until I instruct the above Firm and/or an attorney of that Firm in writing to the contrary

USE ONLY FOR PILLSBURY WINTHROP

00909

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☐ FOR ADDITIONAL INVENTORS see attached page.

☐ See additional foreign priorities on attached page (incorporated herein by reference).

Atty. Dkt. No. P 0282714
(M#)